



# Impella vs intra-aortic balloon pump in patients with acute myocardial infarction complicated with cardiogenic shock: an updated systematic review and meta-analysis

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## Abstract

Cardiogenic shock (CS) is a major cause of mortality in patients with acute myocardial infarction (AMI). Mechanical circulatory support devices like Impella and intra-aortic balloon pump (IABP) manage AMI-CS, but their comparative effectiveness remains unclear. We conducted a meta-analysis following Cochrane and PRISMA guidelines. From the database inception until March 2024, we searched databases including PubMed, Google Scholar, and the Cochrane Library for studies comparing Impella and IABP in AMI-CS patients. Risk ratios (RR) for dichotomous outcomes and mean differences (MD) for continuous outcomes were calculated using a random-effects model. Nine studies involving 18,289 patients were included and the mean age of patients in the Impella group was 64.79 years, and 64.75 years in the IABP group. Short-term mortality showed no significant difference between Impella and IABP (RR: 1.13, 95% CI: 0.84-1.52,  $p=0.42$ ,  $I^2=76\%$ ). Impella was associated with higher risks of hemolysis (RR: 9.46,  $p=0.009$ ), limb ischemia (RR: 3.65,  $p=0.003$ ), transfusion (RR: 2.03,  $p<0.0001$ ), and acute kidney injury (RR: 1.22,  $p=0.04$ ). Meta-regression indicated that peripheral arterial disease, prior PCI, and left ventricular ejection fraction were significant covariates for short-term mortality. Our meta-analysis found no significant difference in short-term mortality between Impella and IABP in AMI-CS patients. In contrast, Impella is associated with higher risks of hemolysis, limb ischemia, transfusion needs, and acute kidney injury. Peripheral arterial disease, prior PCI, and lower LVEF were significantly associated with short-term mortality, with PAD and prior PCI increasing risk, while higher LVEF demonstrated a protective effect.

**Key words:** Impella; intra-aortic balloon pump; cardiogenic shock; meta-analysis.

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## Introduction

Cardiogenic shock (CS) is the most common cause of death in patients with acute myocardial infarction (AMI) and complicates 5-12% of cases despite advancements in supportive medical therapies such as inotropes and early revascularization.<sup>1</sup> It is associated with an in-hospital mortality rate of 15 to 40% and a one-year mortality rate of 25 to 55%.<sup>2-4</sup> Current cardiogenic shock guidelines condone the use of mechanical circulatory support devices such as Impella or intra-aortic bal-

loon pump (IABP) based on observational data suggesting improvement in mortality.<sup>5</sup>

IABP is the most widely used mechanical device for the treatment of AMI.<sup>6</sup> IABP support effectively reduces the left ventricular wall stress and myocardial demand, increases the coronary perfusion pressure, stroke volume, and cardiac output, and ameliorates ischemia, making it a potentially valuable therapy in CS.<sup>6,7</sup> However, in 2013, ACCF/AHA released an updated guideline for patients with ST-elevated myocardial infarction (STEMI), where the recommendation for the placement of IABP

in CS was downgraded from Class I to Class IIa, due to the lack of clear superiority in clinical benefit and reduction of mortality.<sup>8</sup> On the other hand, the Impella® pump (Abiomed, Danvers, MA, USA) is a minimally invasive device that provides excellent left ventricular unloading and full circulatory support.<sup>9</sup> It decreases preload and oxygen consumption, increases myocardial blood flow, and reduces infarction area.<sup>10,11</sup> The Impella LP2.5 is a catheter-based, impeller-driven, axial-flow pump with a maximal flow of 2.5 l/min from the left ventricle to the ascending aorta and can be implanted *via* a percutaneous approach.<sup>12</sup> The survival benefit and safety of Impella vs IABP in acute myocardial infarction complicated with cardiogenic shock (AMI-CS) were investigated in several randomized control trials and observational studies that revealed mixed results.<sup>13</sup>

Given this knowledge gap, we performed this rigorous meta-analysis to assess the procedural and long-term clinical outcomes in patients undergoing Impella vs IABP. This meta-analysis aims to provide valuable insights that enhance the quality of care for patients within the field of interventional cardiology.

## Methods

This meta-analysis and systematic review was conducted according to the established guidelines by Cochrane and Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).<sup>14</sup> Since we used data from already published literature and did not collect any new patient data, this study did not require approval from the institutional review board.

## Literature search and search strategy

The research team conducted a systematic search for the published literature on multiple databases which included PubMed, Google Scholar, and Cochrane Library. We searched for studies published from inception till March 2024 using the keywords (Impella OR percutaneous ventricular assist device OR Intra-aortic balloon pump OR IABP) AND (acute myocardial infarction OR AMI-CS OR STEMI OR NSTEMI) AND (Cardiogenic Shock OR Cardiac Shock). Moreover, we also identified articles from the reference lists of the relevant studies to be included in our library of studies. A detailed search string containing all the pertinent keywords used during the search is outlined in the *Supplementary Table S1*.

## Study selection and eligibility criteria

Duplicate articles were eliminated from all the articles that the search yielded and loaded into EndNote X9 Reference Manager (Clarivate Analytics, Philadelphia, PA, USA). The remaining articles were screened for relevancy through title and abstract by two independent researchers (MR and SB). Full texts of the

shortlisted articles were assessed for the presence of relevant intervention and control groups, outcomes of interest, and methodology. Disagreements were resolved with the consensus of the third author (MA). Studies were selected if they met the following inclusion criteria: i) Impella vs IABP in patients with AMI-CS, ii) patients above 18 years, iii) observational studies or randomized controlled trials (RCTs), and iv) any outcome of interest was reported. Exclusion criteria included: i) case reports, review articles, conference papers, and abstracts, ii) patients under 18 years, iii) single-arm studies, and iv) studies that did not report any outcome of interest.

## Data extraction

Two authors (MA and SA) independently extracted data from the shortlisted studies on an Excel sheet. Important data pertinent to the trial (author name, year) and participants at baseline (sample size, age) were collected. In addition, outcomes were also extracted which included short-term mortality being the primary outcome whereas secondary outcomes included: long-term mortality, stroke, hemolysis, limb ischemia, major bleeding, transfusion, MI, sepsis acute kidney injury, inotropic length of support, and mechanical ventilation. Data reported in the median and interquartile range (IQR) was converted to mean and SD using Wan's method.<sup>15,16</sup>

## Risk of bias and quality assessment

Quality assessment for the included RCTs and observational studies which was done using the Cochrane Risk of Bias tool (RoB 2.0) and Newcastle Ottawa Scale, respectively.<sup>17,18</sup> All the included studies had a low to moderate risk of bias. Detailed quality assessment is provided in the *Supplementary Table S2* and *Figure S1*.

## Statistical analysis

We used Review Manager (V.5.4.1 Cochrane Collaboration, London, UK) to perform the statistical analysis. Generic inverse variance (GIV) was used to derive risk ratios (RR) for dichotomous outcomes and mean differences (MD) were calculated for continuous outcomes with 95% confidence intervals (CIs). A random effects model was used to evaluate all the outcomes. The heterogeneity across pooled studies was assessed using Higgins I<sup>2</sup> statistics. A value of I<sup>2</sup>=25%-50% was considered mild, 50-75% as moderate, and greater than 75% as severe heterogeneity.<sup>19</sup> We performed a sensitivity analysis for the outcomes which showed severe heterogeneity to find the cause of it. Since our meta-analysis did not include more than 10 studies, we did not check generate funnel plots to assess for publication bias. A *p*-value <0.05 was considered significant throughout our analysis.

## Results

### Study selection and characteristics

A comprehensive literature search was conducted and yielded 1159 articles, dated 13-03-2024. Upon removing duplicates, nine studies (three randomized controlled trials, and six observational studies) were included in this meta-analysis. The PRISMA flowchart presents the summary of the literature search (*Supplementary Figure S2*). Nine studies comprised 18,289 patients (6,803 in the Impella group vs 11,486 in the IABP group). The follow-up time ranged from 28 days up to 5 years. The mean age of patients in the Impella group was 64.79 years, and 64.75 years in the IABP group. The baseline characteristics of the included studies are summarized in Table 1.

### Primary outcome

#### Short-term mortality

A meta-analysis of seven studies demonstrated that there was no statistical difference between both groups for the outcome of short-term mortality and the result showed severe heterogeneity (RR: 1.13, 95% CI [0.84,1.52];  $p=0.42$ ,  $I^2=76\%$ ).

#### Assessment of heterogeneity

Sensitivity analysis, which removed one study at a time, revealed that after eliminating Kim *et al.*<sup>5</sup> the substantial heterogeneity in the overall estimate decreased from 76% to 21%, and the results remained insignificant. This helped to explain the high heterogeneity in the plot of short-term mortality (RR 0.98;  $p=0.86$ ,  $I^2=21\%$ , 95% CI (0.82,1.18)).

### Secondary outcomes

All the secondary outcomes are reported in the tabular form in Table 2. Forest plots for secondary outcomes are presented in the supplementary file (*Figures S3-S13*).

### Meta-regression

A meta-regression analysis was conducted to explore potential sources of heterogeneity and assess covariates influencing the effect size of short-term mortality in patients with AMI-CS. Covariates included clinically relevant and commonly reported variables across the studies, such as mean age, percentage of male participants, diabetes mellitus (DM), dyslipidemia, hypertension, left ventricular ejection fraction (LVEF), peripheral arterial disease (PAD), prior CABG, prior MI, prior PCI, prior stroke, and smoking status. The analysis employed a random-effects meta-regression model using restricted maximum like-

**Table 1.** Baseline characteristics of patients in the included studies.

Variables	Alushi <i>et al.</i> <sup>20</sup>	Manzo-Silberman <i>et al.</i> <sup>21</sup>	Ouwneel <i>et al.</i> <sup>22</sup>	Padberg <i>et al.</i> <sup>23</sup>	Pieri <i>et al.</i> <sup>24</sup>	Schrage <i>et al.</i> <sup>25</sup>	Seyfarth <i>et al.</i> <sup>26</sup>	Kim <i>et al.</i> <sup>5</sup>
	Impella	IABP	Impella	IABP	Impella	IABP	Impella	IABP
Number of patients, n	62	54	35	43	24	24	28	36
Age, mean (SD)	71.33±12.902	70±8.378	59.333±4.686	56±12.186	59±11	58±9	66.3±10.7	65.2±11.7
Male, n (%)	44 (71)	41 (76)	29 (83)	35 (81)	20 (83)	18 (75)	20 (71%)	20 (56%)
HTN, n (%)	36 (58)	34 (63)	-	-	6 (29)	4 (20)	12 (43)	26 (72)
DM, n (%)	-	-	-	-	3 (13)	2 (9)	7 (25)	11 (31)
Dyslipidemia, n (%)	36 (58)	38 (70)	-	-	5 (24)	4 (20)	9 (32)	21 (58)
Smoking, n (%)	10 (16)	19 (35)	-	-	6 (32)	11 (61)	3 (11)	18 (50)
LVEF (%), mean (SD)	27.66±11.384	34.33±6.854	26.66±11.594	33.333±1.504	26±1.57	24.66±2.36	21±7	26±8
BMI, mean (SD)	26.66±3.035	26.333±3.808	-	-	26±1.57	24.66±2.36	24.6±3.0	26.0±3.6
CKD, n (%)	12 (19)	8 (15)	-	-	-	-	1 (3.6)	4 (11)
CAD, n (%)	-	-	10 (29)	8 (19)	-	-	-	-
Prior stroke, n (%)	5 (8.1)	3 (3.37)	-	-	1 (4)	0 (0)	2 (7.1)	0 (0)
Prior MI, n (%)	11 (18)	7 (13)	-	-	1 (4)	1 (5)	14 (50)	10 (28)
Peripheral artery disease, n (%)	2 (3.2)	3 (5.6)	-	-	0 (0)	2 (9)	1 (3.6)	4 (11)
Prior PCI, n (%)	15 (24)	7 (13)	-	-	-	-	13 (46)	11 (31)
Prior CABG, n (%)	3 (4.9)	0 (0)	-	-	-	-	1 (3.6)	1 (2.8)
BMI, body-mass-index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; HTN, hypertension; IABP, intra-aortic balloon pump; MI, myocardial infarction; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction.								

likelihood estimation (REML) to account for both within-study and between-study variability. The primary outcome, short-term mortality, was the dependent variable, while the selected covariates were examined as independent variables. The regression coefficients were calculated for each covariate, along with the *p*-values, to determine the strength and statistical significance of associations.

The results revealed that three covariates -PAD, prior PCI, and LVEF- demonstrated a statistically significant association with short-term mortality. Specifically, the presence of PAD and prior PCI was associated with an increased effect size, suggesting a higher risk of short-term mortality, while a higher LVEF showed a protective effect.

The result for meta-regression is summarized in Table 3 and the scatter plots are included in the *Figures S14-S25*.

## Discussion

We conducted an updated meta-analysis that compared the effectiveness of Impella vs IABP in AMI-CS patients. Our summary of results outlined the differences between the two groups across various primary and secondary outcomes. The results revealed no significant differences between Impella

and IABP regarding the primary outcome. However, four secondary outcomes- hemolysis, limb ischemia, transfusion, and acute kidney injury showed significantly higher events in Impella as compared to IABP. Meanwhile, all remaining secondary outcomes were found to be insignificant.

For the outcome of short-term mortality which was statistically insignificant. Our findings align with prior studies, including the IABP-SHOCK II trial, which also reports no significant mortality difference between Impella and IABP despite superior hemodynamic performance with Impella. These results emphasize the need for an individualized approach to mechanical circulatory support (MCS) selection, considering patient-specific factors, device-related complications, and clinical goals beyond immediate hemodynamic stabilization. Both Impella and IABP were effective in improving hemodynamic parameters such as mean arterial pressure and cardiac index. These improvements in hemodynamic stability may have contributed to similar outcomes in terms of mortality.<sup>27</sup> Moreover, the meta-analysis showed that active mechanical support devices led to a reduction in arterial lactate levels, which are associated with better tissue perfusion and may have contributed to comparable mortality rates in both groups.<sup>27</sup> Our results also align with the previous meta-analysis conducted by Moustafa *et al.*, involving 3921 patients.<sup>13</sup> Despite

**Table 2.** Secondary outcomes.

Outcome	Studies	Effect measure (95 % CI)	<i>p</i> -value	I <sup>2</sup>
Long-term mortality	4	RR: 1.13 (0.89, 1.44)	0.33	55%
Stroke	6	RR: 0.87 (0.66, 1.16)	0.34	0%
Hemolysis	3	RR: 9.46 (1.75, 51.22)	0.009	0%
Limb ischemia	5	RR: 3.65 (1.55, 8.61)	0.003	0%
Major bleeding	4	RR: 2.27 (0.92, 5.63)	0.08	62%
Transfusion	2	RR: 2.03 (1.48, 2.79)	<0.0001	0%
Myocardial infarction	4	RR: 0.64 (0.24, 1.17)	0.37	0%
Sepsis	3	RR: 1.25 (0.83, 1.90)	0.29	64%
Acute kidney injury	3	RR: 1.22 (1.01, 1.48)	0.04	68%
Inotropic length of support	4	MD: 0.13 (-0.28, 0.54)	0.53	14%
Mechanical ventilation	3	MD: -0.20 (-37.32, 36.91)	0.99	0%

CI, confidence interval; I<sup>2</sup>, heterogeneity; MD, mean difference; RR, risk ratio.

**Table 3.** Meta-regression for short-term mortality.

Variable	Coefficient	<i>p</i> -value
Mean age	-0.0121	0.6125
Male sex %	-0.0205	0.3217
Diabetes mellitus	0.0149	0.3013
Hypertension	-0.0045	0.6658
Smoking	0.0047	0.6714
Dyslipidemia	-0.0059	0.6100
Prior stroke	0.0200	0.6269
Prior myocardial infarction	0.0085	0.3436
Peripheral artery disease	0.0518	0.0021
Prior percutaneous coronary intervention	0.0108	0.0060
Prior coronary artery bypass grafting	0.0632	0.2679
Left ventricular ejection fraction	-0.356	0.0130

differences in the mechanisms of action between Impella and IABP, both devices may have provided similar levels of circulatory support in the context of cardiogenic shock. In the IMPRESS trial, the causes of insignificant long-term mortality differences between the Impella and IABP groups were primarily attributed to brain damage and refractory cardiogenic shock.<sup>22,28</sup> Specifically, the primary cause of death at 6 months in both groups was brain damage, accounting for 46% of the deceased patients, and death due to refractory cardiogenic shock occurred in 29% of the deceased patients.<sup>22</sup> We found no significant difference between the two groups for stroke and these results are similar to the findings of the previous meta-analysis, and a possible explanation for the similar stroke rate in both Impella and IABP is that their presence in the left ventricular apex and aorta, respectively, increases the risk of clot formation, leading to embolization and stroke complications and the insertion of IABP into the aorta causes vascular trauma or dissection, leading to impaired blood flow and potentially stroke and prolonged immobilization in IABP increases the risk of venous thrombosis and subsequent stroke.<sup>29,30</sup>

Our pooled analysis demonstrated a higher incidence of hemolysis in Impella compared to IABP which can be because the Impella device involves direct contact with blood, which can lead to mechanical stress on red blood cells, causing them to rupture and release hemoglobin into the bloodstream, and the design of the Impella pump, which involves continuous axial flow, can contribute to shear stress on blood cells, potentially leading to hemolysis and patients undergoing Impella placement may have a higher volume of contrast exposure, which can increase the risk of contrast-induced nephropathy and acute kidney injury, factors that are associated with hemolysis.<sup>31</sup> Furthermore, the Impella device may be associated with device-related complications such as infection, access site hemorrhage, and hematoma, which can contribute to hemolysis.<sup>31</sup> Our results also align with the previous meta-analysis conducted by Moustafa *et al.*<sup>13</sup> The higher incidence of limb ischemia associated with Impella compared to IABP can be attributed to several factors. Firstly, the Impella device is inserted through the femoral artery or axillary artery, which may pose a higher risk of vascular complications compared to the percutaneous insertion of the IABP and the insertion of the Impella device, especially through the axillary artery with a graft, may result in local vascular trauma or complications, increasing the risk of limb ischemia and Impella therapy often requires more intense anticoagulation compared to IABP, which can predispose patients to bleeding complications, including limb ischemia.<sup>32</sup> Furthermore, the Impella device is a non-pulsatile axial flow pump that propels blood into the ascending aorta, which may affect vascular perfusion differently compared to the counter-pulsation mechanism of the IABP and prolonged use of the Impella device may increase the risk of vascular complications, including limb ischemia, compared to the temporary support provided by the IABP.<sup>32</sup>

Our finding of insignificant major bleeding aligns with the

studies by Pieri *et al.* and Boudoulas *et al.*<sup>24,33</sup> Approximately 65.3% of bleeding events were due to vascular access site/procedural issues, while 30.7% were related to gastrointestinal bleeding, and 3.8% to genitourinary bleeding.<sup>33</sup> The higher need for blood transfusions in patients receiving Impella support compared to those receiving IABP support concurs with the findings of Thakkar *et al.* which could be due to the association of the Impella device with a higher incidence of hemolysis, resulting in decreased hemoglobin levels and the need for blood transfusions to maintain adequate oxygen-carrying capacity in the blood.<sup>31</sup> Furthermore, the Impella device requires a larger access catheter size compared to IABP, potentially increasing the risk of vascular complications such as access site hemorrhage and hematoma, which may necessitate blood transfusions.<sup>31</sup> Additionally, the Impella device has been linked to a higher rate of bleeding complications, leading to significant blood loss and the need for blood transfusions and patients receiving Impella support may be at a higher risk of device-related infections, which can lead to systemic complications requiring blood transfusions.<sup>31</sup> In addition to that, our analysis found no significant difference in reinfarction rates between Impella and IABP. Implantation of IABP and left ventricular assisting devices (LVADs) have been shown to induce systemic inflammatory response syndrome (SIRS).<sup>34</sup> SIRS has been linked to various complications, including ischemia-reperfusion injury after PCI, infection, and an overactive immune response to the catheter of IABP or LVADs.<sup>35</sup> This may lead to the production of toxic nitric oxide and superoxide ions, resulting in sustained myocardial cell injury.<sup>36</sup> Our finding of no significant difference in sepsis rates between the two groups aligns with the results of Pieri *et al.*<sup>24</sup> The higher incidence of AKI in patients receiving Impella compared to IABP is due to IABP providing diastolic augmentation of renal perfusion, which may help reduce pre-renal AKI rates by improving renal blood flow.<sup>31,37</sup> Patients undergoing Impella placement may be exposed to a higher volume of contrast, increasing the risk of contrast-induced nephropathy and subsequent AKI.<sup>31,38</sup> Impella use has been linked to a higher incidence of hemolytic anemia due to mechanical hemolysis, which may potentially contribute to AKI rates.<sup>39</sup> This finding aligns with prior studies, reported an increased risk of AKI and other adverse outcomes associated with Impella use.<sup>40,41</sup>

## Limitations

The limitations of our meta-analysis comparing the effectiveness of Impella vs IABP in AMI-CS patients are noteworthy. Firstly, there is considerable heterogeneity in study design, patient populations, and clinical settings, which can introduce bias and limit the generalizability of our findings. The included studies also exhibit variability in outcome definitions and reporting, complicating accurate data pooling and potentially leading to inconsistencies. Additionally, many studies had relatively short follow-up periods, leaving long-



term efficacy and safety unclear. Small sample sizes in some studies may limit statistical power, affecting the robustness of the results. Variations in management protocols, including differences in concomitant medical therapies and anticoagulation, add another layer of complexity. The observational nature of some studies introduces selection bias, influenced by patient-specific factors and clinician preferences. The technology and clinical experience with Impella and IABP have evolved, and earlier studies may not reflect current practices. The learning curve and surgeon experience with these devices, particularly with newer Impella models, also impact outcomes. Lack of blinding in many studies could introduce performance and detection bias. Inconsistent reporting of adverse events might lead to underestimation of device-related complications. Furthermore, variations in patient demographics and the use of different Impella devices could contribute to outcome differences. Lastly, residual confounding by unmeasured variables, such as operator experience, institutional protocols, and patient socioeconomic status, cannot be ruled out, potentially influencing the observed outcomes.

## Conclusions

Based on our meta-analysis, there was no significant difference between Impella and IABP in terms of short-term mortality in AMI-CS patients. However, secondary outcomes revealed that Impella was associated with significantly higher rates of hemolysis, limb ischemia, transfusion, and acute kidney injury compared to IABP. Meta-regression identified peripheral arterial disease, prior PCI, and left ventricular ejection fraction as significant covariates influencing short-term mortality. These findings suggest that while both devices offer similar short-term survival benefits, Impella may carry a higher risk of complications.

## Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas: took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Ethics approval and consent to participate

Not applicable.

## Availability of Data and Materials

The dataset supporting the conclusions of this article is included in this article.

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*Online supplementary material:*

*Table S1. Search strategy used in each database*

*Table S2. Newcastle-Ottawa quality assessment scale for cohort studies*

*Figure S1. Risk of bias for the included randomized-controlled-trials*

*Figure S2. PRISMA flowchart*

*Figure S3. Forest plot for long-term mortality*

*Figure S4. Forest plot for stroke*

*Figure S5. Forest plot for hemolysis*

*Figure S6. Forest plot for limb ischemia*

*Figure S7. Forest plot for major bleeding*

*Figure S8. Forest plot for transfusion*

*Figure S9. Forest plot for myocardial infarction*

*Figure S10. Forest plot for sepsis*

*Figure S11. Forest plot for acute kidney injury*

*Figure S12. Forest plot for the inotropic length of support*

*Figure S13. Forest plot for the mechanical ventilation*

*Figure S14. Scatter plot for mean age*

*Figure S15. Scatter plot for male sex %*

*Figure S16. Scatter plot for diabetes mellitus*

*Figure S17. Scatter plot for hypertension*

*Figure S18. Scatter plot for smoking*

*Figure S19. Scatter plot for dyslipidemia*

*Figure S20. Scatter plot for prior stroke*

*Figure S21. Scatter plot for prior MI*

*Figure S22. Scatter plot for PAD*

*Figure S23. Scatter plot for prior PCI*

*Figure S24. Scatter plot for prior CABG*

*Figure S25. Scatter plot for LVEF*